

Amendments to the Claims:

Listing of Claims:

Claims 1-18 (canceled)

Claim 19 (new): Method for identifying and selecting an oligonucleotide which is capable of modulating regulatory RNA-ligand interactions, comprising

- (a) defining and selecting a secondary structure element of an RNA molecule which is required for the recognition by a ligand, e.g. protein,
- (b) calculating the thermodynamic probability of the secondary structure element of step a) in the secondary structure ensemble of said RNA,
- (c) calculating the thermodynamic probability of the secondary structure element of step a) in the secondary structure ensemble of said RNA hybridized to an at least partly reverse complementary oligonucleotide,
- (d) identifying and selecting an oligonucleotide that changes the thermodynamic probability of said secondary structure element beyond a defined probability threshold, and optionally validating experimentally this oligonucleotide as defined in the following steps (e), (f) and (g),
- (e) providing an oligonucleotide as determined in step (d),
- (f) hybridizing an RNA comprising said secondary structure element of step (a) to an oligonucleotide of step (e), and
- (g) determining the effect of said hybridization on the thermodynamic probability of said secondary structure element and further selecting the oligonucleotide capable of modulating regulatory RNA ligand interactions by hybridizing to said RNA.

Claim 20 (new): The method of Claim 19, for identifying an oligonucleotide capable of boosting or silencing a target gene expression.

Claim 21 (new): The method of Claim 19, wherein said ligand is HuR and said RNA molecule comprising a secondary structure required for the recognition by HuR is an mRNA.

Claim 22 (new): The method of Claim 21, wherein said mRNA is IL-2.

Claim 23 (new): The method of Claim 21, wherein said mRNA is TNF α .

Claim 24 (new): Method of claim 22, wherein the

oligonucleotide has a sequence selected at step (d) from the group consisting of

SEQ ID NO 1:AAGGCCTGATATGTTTTAAG,
SEQ ID NO 2:AATATAAAATTTAAATATTT,
SEQ ID NO 3:TAGAGCCCCTAGGGCTTACA,
SEQ ID NO 4:TGAAACCATTTTAGAGCCCC,
SEQ ID NO 5:AAGGCCUGAUUUGUUUUAAG,
SEQ ID NO 6:AAUAUAAAAUUUAAAUUUU,
SEQ ID NO 7: UAGAGCCCCUAGGGCUUACA,
SEQ ID NO 8: UGAAACCAUUUUAGAGCCCC.

Claim 25 (new): Method of claim 23, wherein the

oligonucleotide has a sequence selected at step (d) from the group consisting of

SEQ ID NO 9: TCGGCCAGCTCCACGTCCCG,
SEQ ID NO 10: TCTGGTAGGAGACGGCGATG,
SEQ ID NO 11: ACGGCGATGCGGCTGATGGT,
SEQ ID NO 12: TTCTGGAGGCCCCAGTTTGA,
SEQ ID NO 13: ATTCCAGATGTCAGGGATCA, and
SEQ ID NO 14: ATCACAAGTGCAAACATAAA.

Claim 26 (new): Assay for identifying an agent that modulates the effect of the hybridization of an oligonucleotide which can be identified by the method of Claim 19, to an RNA molecule comprising

- (a) hybridizing an RNA comprising a secondary structure element which is required for recognition by a ligand to an oligonucleotide that changes the thermodynamic probability of said secondary structure element beyond a defined probability threshold in the presence and in the absence of a candidate compound,
- (b) determining the effect of hybridization of said RNA to said oligonucleotide in the presence and in the absence of said candidate compound,
- (c) identifying an agent which modulates the effect of hybridization.

Claim 27 (new): Assay for identifying an agent that mimics the effect of hybridization of an RNA molecule to an oligonucleotide which can be identified by the method of Claim 19, comprising

- (a) hybridizing an RNA comprising a secondary structure element which is required for recognition by a ligand to an oligonucleotide that changes the thermodynamic probability of said secondary structure element beyond a defined probability threshold

- (b) hybridizing an RNA comprising a secondary structure element which is required for recognition by a ligand to a candidate compound which is expected to have a similar effect as an oligonucleotide which can be identified by the method of Claim 19,
- (c) determining the effect of hybridization for steps (a) and (b), and
- (d) identifying the agent among the candidate compounds which mimic the effect of hybridization of step (a).

Claim 28 (new): Assay of Claim 26, wherein the effect of hybridization is determined by measuring a signal which is related to the effect of hybridization, which effect is selected from the group consisting of changes in secondary ANA structure, tertiary RNA structure, RNA-ligand affinity, RNA oligo- or multimerization, ligand oligo- or multimerization, conformational change of the ligand, efficiency of a downstream effect of RNA-ligand recognition, RNA splicing, covalent RNA modifications, RNA localization, RNA stability, RNA translation and protein expression profiles.

Claim 29 (new): Assay of Claim 26 wherein the RNA is an mRNA.

Claim 30 (new): Assay of Claim 26, wherein said ligand is HuR and said RNA molecule comprising a secondary structure required for the recognition by HuR is an mRNA.

Claim 31 (new): Use of an assay of Claim 26 for high throughput screening.

Claim 32 (new): Agent identified by an assay of Claim 26 for use as a pharmaceutical.

Claim 33 (new): An oligonucleotide that changes the thermodynamic probability of a secondary structure element beyond a defined probability threshold identified by a method of claim 19.

Claim 34 (new): An oligonucleotide having a sequence selected from the group consisting of
SEQ ID NO 1: AAGGCCTGATATGTTTAAAG,
SEQ ID NO 2: AATATAAAATTTAAATATTT,
SEQ ID NO 3: TAGAGCCCCTAGGGCTTACA,
SEQ ID NO 4: TGAAACCATTTTAGAGCCCC,
SEQ ID NO 5: AAGGCCUGAUUGUUUUAAG,
SEQ ID NO 6: AAUAUAAAUUUAAAUUUU,
SEQ ID NO 7: UAGAGCCCCUAGGGCUUACA,
SEQ ID NO 8: UGAAACCAUUUUAGAGCCCC.
SEQ ID NO 9: TCGGCCAGCTCCACGTCCCG,

SEQ ID NO 10: TCTGGTAGGAGACGGCGATG,
SEQ ID NO 11: ACGGCGATGCGGCTGATGGT,
SEQ ID NO 12: TTCTGGAGGCCCCAGTTTGA,
SEQ ID NO 13: ATTCCAGATGTCAGGGATCA, and
SEQ ID NO 14: ATCACAAGTGCAAACATAAA.

Claim 35 (new): An oligonucleotide identified by a method of claim 19 in which the oligonucleotide is an RNA or DNA molecule with any chemical modification.

Claim 36 (new): An oligonucleotide according to claim 34 in which the oligonucleotide is an RNA or DNA molecule with any chemical modification.

Claim 37 (new): An oligonucleotide identified by a method of Claim 19 in which the oligonucleotide is a peptoid nucleic acid or a locked nucleic acids molecule.

Claim 38 (new): An oligonucleotide according to claim 34 in which the oligonucleotide is a peptoid nucleic acid or a locked nucleic acids molecule.

Claim 39 (new): Use of an oligonucleotide of Claim 33 for manipulating regulatory RNA-ligand interactions.

Claim 40 (new): Use of an oligonucleotide of Claim 33, for manipulating the expression of a gene, for example for boosting or silencing gene expression.

Claim 41 (new): Use of an oligonucleotide of Claim 33 for influencing the stability of an RNA molecule.

Claim 42 (new): Use of an oligonucleotide identified according to the method of Claim 23, for increasing TNF α mRNA stability.

Claim 43 (new): Use of an oligonucleotide identified according to the method of Claim 23, for increasing TNF α gene expression.

Claim 44 (new): Use of an oligonucleotide selected among the group consisting of SEQ ID NO 1, 2, 3 and 4, for increasing IL2 mRNA stability and/or IL2 gene expression.

Claim 45 (new): Use of an oligonucleotide of SEQ ID NO14 for increasing TNF α mRNA stability and/or TNF α gene expression.

Claim 46 (new): Pharmaceutical composition comprising an agent identified by an assay of Claim 26, along with at least one pharmaceutical excipient.

Claim 47 (new): Pharmaceutical composition comprising an agent identified by an oligonucleotide according to Claim 33, along with at least one pharmaceutical excipient.